

Appl. No. : 09/991,721
Filed : November 13, 2001

AMENDMENTS TO THE CLAIMS

1. **(Currently amended)** A composition of matter ~~A tumor cell~~ comprising a recombinant WR strain vaccinia virus, said vaccinia virus comprising ~~a vaccinia virus expression vector comprised of~~ a mutation in a thymidine kinase (TK) gene of the genome of said vaccinia virus to produce a negative TK phenotype and comprising ~~comprised of~~ a mutation in at least one vaccinia virus growth factor (VVGF) gene of the genome of said vaccinia virus to produce a negative VVGF phenotype, ~~wherein said tumor cell is present in vivo in a mammal.~~

2. **(Currently amended)** The composition of claim 1, ~~wherein said vaccinia virus~~
~~The tumor cell of claim 1,~~ wherein said vector further comprises an exogenous nucleotide sequence.

3. **(Currently amended)** The composition ~~The tumor cell~~ of claim 1, wherein said negative thymidine kinase phenotype results from a vaccinia virus thymidine kinase gene containing a deletion of nucleic acid sequence.

4. **(Currently amended)** The composition ~~The tumor cell~~ of claim 1, wherein said negative thymidine kinase phenotype results from a vaccinia virus genome from which a thymidine kinase gene is deleted.

5. **(Currently amended)** The composition ~~The tumor cell~~ of claim 1, wherein said negative thymidine kinase phenotype results from a vaccinia virus thymidine kinase gene containing an insertion of nucleic acid sequence.

6. **(Currently amended)** The composition ~~The tumor cell~~ of claim 1, wherein said negative thymidine kinase phenotype results from a vaccinia virus thymidine kinase gene containing a substitution of nucleic acid sequence.

7. **(Currently amended)** The composition ~~The tumor cell~~ of claim 1, wherein said negative vaccinia virus growth factor phenotype results from at least one vaccinia virus growth factor gene containing a deletion of nucleic acid sequence.

8. **(Currently amended)** The composition ~~The tumor cell~~ of claim 7, wherein said deletion comprises a deletion of the EGF-receptor binding site of said vaccinia virus growth factor gene.

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9. (Currently amended) The composition ~~The tumor cell~~ of claim 1, wherein said negative vaccinia virus growth factor phenotype results from a vaccinia virus genome from which at least one vaccinia virus growth factor gene is deleted.

10. (Currently amended) The composition ~~The tumor cell~~ of claim 1, wherein said negative vaccinia virus growth factor phenotype results from at least one vaccinia virus growth factor gene containing an insertion of nucleic acid sequence.

11. (Currently amended) The composition ~~The tumor cell~~ of claim 1, wherein said negative vaccinia virus growth factor phenotype results from at least one vaccinia virus growth factor gene containing a substitution of nucleic acid sequence.

12. (Currently amended) The composition ~~The tumor cell~~ of claim 2, wherein said exogenous nucleotide sequence is selected from the group consisting of tumor suppressor genes, cytotoxic genes, cytostatic genes, cytokines, suicide genes, and antigen encoding genes.

13. (Currently amended) The composition ~~The tumor cell~~ of claim 12, wherein said tumor suppressor gene is selected from the group consisting of WT1, p53, p16, Rb, and BRCA1.

14. (Canceled)

15. (Currently amended) The composition of claim 1, wherein said vaccinia virus ~~The tumor cell of Claim 1, wherein said vaccinia virus expression vector~~ is produced by a virus particle containing a virus genome, wherein expression of said genome produces a vaccinia virus with a negative thymidine kinase phenotype and a negative vaccinia virus growth factor phenotype.

16. (Canceled)

17. (Currently amended) The composition of claim 1, wherein said vaccinia virus ~~The tumor cell of Claim 1, wherein said vaccinia virus expression vector~~ is constructed such that the gene for *E. coli lacZ* is inserted into the thymidine kinase (TK) or virus growth factor (VGF) site.

18. (Currently amended) The composition of claim 1, wherein said vaccinia virus ~~The tumor cell of Claim 1, wherein said vaccinia virus expression vector~~ is constructed such that the gene for enhanced green fluorescent protein (EGFP) is inserted into the thymidine kinase (TK) or virus growth factor (VGF) site.

19.-24 (Canceled)

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25. (Currently amended) A product made by the method of:

providing a WR strain vaccinia virus genome and constructing a recombinant WR strain vaccinia virus ~~a vaccinia virus expression vector~~ by;

mutating at least one vaccinia virus growth factor gene of said vaccinia virus genome to produce a negative vaccinia virus growth factor phenotype; and

mutating a thymidine kinase gene of said vaccinia virus genome to produce a negative thymidine kinase phenotype, whereby a recombinant WR strain vaccinia virus is constructed ; and

~~introducing said vaccinia virus expression vector into a tumor cell, wherein said tumor cell is present in vivo in a mammal and does not encompass said mammal.~~

26-44. (Canceled)

45. (New) The composition of claim 2, wherein said exogenous nucleotide sequence is selected from the group consisting of cystic fibrosis transmembrane regulator (CFTR), Factor VIII, low density lipoprotein receptor, beta-galactosidase, alpha-galactosidase, beta-glucocerebrosidase, insulin, parathyroid hormone, and alpha-1-antitrypsin.

46. (New) The composition of claim 2, wherein said exogenous nucleotide sequence is introduced to inactivate said TK gene.

47. (New) The composition of claim 2, wherein said exogenous nucleotide sequence is introduced to inactivate said VVGF gene.

48. (New) The composition of claim 12, wherein said exogenous nucleotide sequence is a cytokine.

49. (New) The composition of claim 12, wherein said exogenous nucleotide sequence is a suicide gene.

50. (New) The composition of claim 2, wherein said exogenous nucleotide sequence is an imaging agent.